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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/373,403	08/12/1999	WILLIAM R. ARATHOON		2534

7590 04/30/2009

Ginger Dreger Goodwin Procter LLP
1811 Lytto Avenue
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EXAMINER
HOLLERAN, ANNE L

ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
04/30/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/373,403	ARATHOON ET AL.	
	Examiner	Art Unit	
	ANNE L. HOLLERAN	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *56-73 and 75-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *56-73 and 75-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/2/2009 has been entered.

The amendment filed 3/2/2009 is acknowledged. Claim 74 was canceled.

Claims 56-73 and 75-77 are pending and examined on the merits.

Claim Rejections Withdrawn:

The rejection of claims 56, 58-68, 70, 71 and 73-76 under 35 U.S.C. 103(a) as being obvious over Carter-B (WO 96/27011; published 6 Sep., 1996; cited in IDS) in view of de Kruif-A (de Kruif, J. et al. The Journal of Biological Chemistry, 271 (13): 7630-7634, 1996; cited in IDS) and further in view of de Kruif-B (de Kruif, J. et al, J. Mol. Biol., 248: 97-105, 1995; cited in IDS) is withdrawn in view of the amendment to the claims reciting multispecific antibodies comprising at least four polypeptides so that the claims do not read on dimeric scFvs.

The rejection of claims 56, 57, 67 and 69 under 35 U.S.C. 103(a) as being unpatentable over Hu (Hu, S.-z., et al., Cancer Research, 56: 3053-3061, 1996) in view of de Kruif-A (supra)

and further in view of de Kruif-B (supra) is withdrawn in view of the amendment to the claims reciting multispecific antibodies comprising at least four polypeptides so that the claims do not read on dimeric scFvs.

Claim Rejections Maintained and New Grounds of Rejection:

Claim Objections

Claim 70 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 70 does not appear to further limit claim 67 from which it depends, because the limitation that the first and second polypeptide each comprise an antibody constant domain is already present in claim 67, from which claim 70 depends.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 56-73 and 75-77 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 56, 67 and 73 are indefinite because "one of the heavy chain variable domains" lacks antecedent basis.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 73 and 75-77 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

The originally filed claims recited a method for preparing a multispecific antibody comprising a first polypeptide and at least one additional polypeptide, where the first and additional polypeptides each comprise a binding domain comprising a heavy chain and a light chain, wherein the variable light chains of the first and additional polypeptides comprise a common sequence.

Instant claims 73 and 75-77 are drawn to methods of preparing multispecific antibodies where the light chains are different because claim 37 recites a third and fourth polypeptide each comprising a light chain variable domain, wherein the light chain variable domains have at least 98% sequence identity and/or only differ from each other at amino acid positions outside of the CDR regions. Therefore, claims 73 and 75-77 recite methods for making multispecific antibodies where the light chain variable domains are not identical.

The specification at page 10 teaches that a strategy is provided by the instant invention which provides a common variable light chain to interact each of the heteromeric variable heavy chain regions of the bispecific antibody. At page 12, the specification teaches: "It is disclosed herein that the preparation of a desired heteromultimeric multispecific antibody is enhanced when a common light chain is provided to pair with each of the variable heavy chains of the multispecific antibody. Use of a common variable light chain reduces the number of monomers that must correctly pair to form the antigen binding domains by limiting the number of light chains from two or more light chains (in a bispecific or multispecific antibody, respectively, prior to disclosure of the instant invention) to one light chain (in a multispecific antibody of the invention; see Fig. 1C)." The specification at page 21 defines "common light chain" or "common amino acid sequence of the light chain" as referring to the amino acid sequence of the light chain in the multispecific antibody of the invention.

In light of the originally filed claims, and the teachings of the specification, it does not appear that applicants were in possession of methods for making multispecific antibodies having light chains that are different from each other and wherein the different light chains are interchangeable for pairing with heavy chain variable domains of the multispecific antibodies made by the currently claimed methods ("wherein the multispecific antibody comprises a first light chain variable domain and a second light chain variable domain and said first binding domain binds said first molecule whether said first binding domain comprises the first light chain variable domain or the second light chain variable domain, and said second binding domain binds said second molecule whether said second binding domain comprises the second light chain variable domain or the first light chain variable domain.") Other instances in the

specification that indicate that applicant conceived of methods of making bispecific antibodies where all of the binding domains comprise a light chain having the same sequence is found at page 12, line 15-line 24; page 13, lines 6-13; page 16, line 1-15; page 56, lines 13-29; page 95, lines 25-28; and page 103, lines 5-8.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 73, 75 and 76 are rejected under 35 U.S.C. 102(b) as being anticipated by Merchant (Merchant, A.M. et al. Nature Biotechnology, 16: 677-681, 1998, July; cited in IDS).

Priority for the instant claims is denied because the disclosure of the parent application 08/850,058 does not support the claimed inventions. Specifically, the claimed inventions of the instant application comprise methods of making multispecific antibodies where the resultant antibodies have different light chains. In contrast the disclosures of parent application 08/850,058 supports methods where the light chains of the at least two binding domains are the same. Therefore, the filing date of instant application 8/12/1999 is used to compare with prior art.

Merchant teaches methods comprising expressing in HEK293 cells nucleic acid sequences encoding a common immunoglobulin light chain and different immunoglobulin heavy

chains, where the resultant antibodies comprise a bispecific antibody with one binding specificity to Her-3 and the other to Mpl (see page 679, right column). Therefore, Merchant teaches methods and host cells that are the same as that claimed.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran
Patent Examiner
March 29, 2009
/Alana M. Harris, Ph.D./
Primary Examiner, Art Unit 1643